PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DNT-3PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US04/23483	International filing date *(day/month/year)* 21 July 2004 (21.07.2004)	Priority date *(day/month/year)* 21 July 2003 (21.07.2003)
International Patent Classification (IPC) or national classification and IPC IPC(7): B05D 7/00, 7/24 and US Cl.: 427/162, 212, 214, 215, 216, 220; 257/E29.071		
Applicant DENDRITIC NANOTECHNOLOGIES, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 6 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____ , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☒ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19 February 2005 (19.02.2005)	27 May 2005 (27.05.2005)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Tim Meeks Telephone No. (571) 272-1700

Form PCT/IPEA/409 (cover sheet)(January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/23483

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-6 and 8-21 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* 7 received by this Authority on 23 May 2005 (23.05.2005)

☒ the claims:
pages NONE as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* 22-26 received by this Authority on 23 May 2005 (23.05.2005)

☒ the drawings:
pages 1-8 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☒ the claims, Nos. 37-50
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/23483

Box No. II Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☒ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
The priority claim is considered invalid because none of the claims are supported by the priority application.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US04/23483

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Inventive Step (IS)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Industrial Applicability (IA)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO

2. Citations and Explanations (Rule 70.7)
Please See Continuation Sheet

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 10, 11, 13, 14, 22, 23, 27, 28, 30, 31, 33, and 34
The opinion as to Novelty was negative (No) with respect to claims 1-9, 12, 15-21, 24-26, 29, 32, 35, and 36
The opinion as to Inventive Step was positive (Yes)with respect to claims NONE
The opinion as to Inventive Step was negative(NO) with respect to claims 1-36
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-36
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE

V. 2. Citations and Explanations:
This reasoned statement is drawn to the claims (1-36) presented in the response filed on 5/23/2005.

Claims 1 - 9, 12, 15-21, 24-26, 29, 32, 35, and 36 lack novelty under PCT Article 33(2) as being anticipated by Peng et al. (US 2004/0101976 A1).
Regarding independent Claims 1 and 2, Peng et al. teaches a method of stabilizing semiconductor, metal, and/or metal salt nanoparticles by contacting organic dendrons containing single focal point functional groups with colloidal solutions of the aforementioned nanoparticles to react with the surfaces of the nanoparticles and obtain stabilized, dendronized nanoparticles (Abstract, Figures 1-6, paragraphs [0018]-[0066], and Claims 1-23), wherein the focal point group is phosphine or phosphine oxide (paragraph [0062], and Claims 12 and 23). Regarding independent Claim 12, Peng et al. also teaches the corresponding composition of matter comprising a colloidal solution of semiconductor, metal, or metal salt nanoparticles having outside surfaces with dendrons attached thereto, the attachment comprising a linking group selected from the group of phosphorus in the form of a phosphine or a phosphine oxide (Abstract, Figures 1-6, paragraphs [0018]-[0066], and Claims 1-23). Regarding Claims 3 and 4, Peng et al. also teaches that the nanoparticles are passivated prior to contacting them with the dendrons (paragraph [0061]). Regarding Claims 5 - 8, Peng et al. also teaches that the outside surfaces of the dendrons contain functional groups such as hydrophilic groups, hydrophobic groups, reactive groups, and/or passive groups (Figures 3-5; paragraphs [0045], [0046], [0049] - [0051], and Claims 6, 7, and 11). Regarding Claim 9, Peng et al. also teaches that the reactive groups are selected from the group recited by the applicant (paragraphs [0049], [0050], and Claims 11 and 22). Regarding Claims 15 - 21, 24 - 26, and 29, Peng et al. also teaches that the nanoparticle core is iron, gold, copper, platinum, palladium, cobalt, nickel, iron oxide, CdSe, CdS, or CdTe (paragraphs [0042], [0043]; Claims 9 and 20). Regarding Claims 32 and 35, Peng et al. also teaches that the composition of matter is used for drug delivery (paragraph [0065]). Regarding Claim 36, Peng et al. also teaches using the composition on the manner claimed by the applicant (paragraphs [0008], [0056], [0059], [0062], and [0065]).

Claims 10, 11, 13, 14, 22, 23, 27, 28, 30, 31, 33, and 34 have novelty because each and every limitation of the aforementioned claims is not taught by a single reference.

Claims 10, 11, 13, 14, 22, 23, 27, 28, 30, 31, and 33 lack an inventive step under PCT Article 33(3) as being obvious over Peng et al. (US 2004/0101976 A1).
Peng et al. teaches all the limitations of Claims 10, 11, 13, and 14 as set forth above, except for a method / composition wherein the

Supplemental Box

single point phosphine or phosphine oxide of the dendron has the specific chemical formula claimed by the applicant. However, Peng et al. does teach using single point phosphine and phosphine oxide containing dendrons in general to bind with the nanoparticles (paragraph [0062], and Claims 12 and 23), and teaches that the specific dendron that is used in the process or composition is not limited and can be tailored depending on what type of nanoparticle is to be treated (paragraphs [0034] and [0066]). Therefore, it would have been obvious to one of ordinary skill in the art to utilize any specific organic dendron out of the group of organic dendrons taught by Peng et al. (e.g., phosphine and phosphine oxide containing dendrons), including the specific organic dendrons claimed by the applicant, with the reasonable expectation of successfully and advantageously achieving the goal of Peng et al. (i.e., producing high quality dendronized nanocrystals), regardless of the exact chemical formula of the phosphine or phosphine oxide point group used to attach the dendrons to the nanocrystals. Regarding Claims 22, 23, 27, 28, 30, and 31, Peng et al. does not explicitly teach that the nanoparticle is zinc, cadmium, CdSe/CdS, CdSe/ZnS, CdTe/CdS, or CdTe/ZnS. However, the process and composition of Peng et al. is broadly directed to metallic and semiconductor based nanoparticles / nanocrystals in general, including various combinations of the aforementioned elements (paragraphs [0042] and [0043]). Therefore, it would have been obvious to one of ordinary skill in the art to dendronize any nanoparticle (including those claimed by the applicant) out of the broad genus of nanoparticles disclosed by Peng et al. with the reasonable expectation of successfully and advantageously producing high quality nanoparticles stabilized with dendrons, regardless of the exact chemical composition of the nanoparticles. The type of nanoparticle treated by the process of Peng et al. would, of course, depend on the intended end-use of the nanoparticle. Regarding Claim 33, Peng et al. teaches that the nanoparticle core can be a magnetic material such as iron (paragraph [0043]), and using dendronized magnetic nanoparticles in general as MRI agents (paragraph [0065]). Therefore, it would have been obvious to one of ordinary skill in the art to utilize a dendronized iron nanoparticle as an MRI agent because the iron core is magnetic, which is a property desired by Peng et al. in the context of using nanoparticles as MRI agents.

Claim 34 lacks an inventive step under PCT Article 33(3) as being obvious over Peng et al. (US 2004/0101976 A1) in view of West et al. (US 2003/0093092 A1).
Peng et al. teaches all the limitations of Claim 34 as set forth above, except for using the dendronized gold nanoparticle in a gene gun. However, Peng et al. does teach that the nanoparticle can be gold and can be utilized in biomedical applications in general. West et al. teaches that one application for a nanoparticle is to target "sub-epidermis" tissue through the use of a gene gun (paragraph [0081]). It would have been obvious to one of ordinary skill in the art to use the dendronized nanoparticles of Peng et al. in a gene gun, as taught by West et al., in order to reap the benefits of dendronizing the nanoparticles in a specific biomedical application (i.e., stabilizing the nanoparticles against aggregation, deterioration, etc.). Such a benefit would be applicable, regardless of the specific biomedical application of the nanoparticle.

Claims 1 - 36 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry (e.g., the biomedical, chemical, or optical industry).

The arguments filed on 5/23/2005 have been fully considered and are discussed below:
(1) Regarding the claim for priority based on U.S. provisional application 60/488,909, the applicant argues that (a) the use of phosphorous in place of sulfer, (b) the use as an MRI agent, and (c) the use as a gene gun are disclosed in the priority document. The applicant then requests that the priority claim be allowed "for all other claims not concerned with Items 1 and 3 above". This argument is not convincing, and the priority claim with respect to Claims 1-36 is considered invalid. All the claims require that the nanoparticles be in colloidal solution, a limitation that is not disclosed in 60/488,909. As such, none of the claims is fully supported by the prior provisional application. Regarding (a) above, the general disclosure of using dendrimers "containing phosphorus atoms" in the priority document does not adequately support Claims 1-36, which specifically require phosphine or phosphine oxide focal point groups. Regarding (b) above, the general disclosure of the possible paramagnetic property of the functionalized quantum dots does not adequately support Claim 33, which specifically requires using a dendronized iron nanoparticle core as an MRI agent. Regarding (c) above, the use in a gene gun is disclosed but not in the context of a gold nanoparticle, as required by Claim 34.

(2) Regarding the "certain defects" and "claim observations", the amendments and comments filed on 5/23/2005 are convincing and sufficient to remove the previous objections.

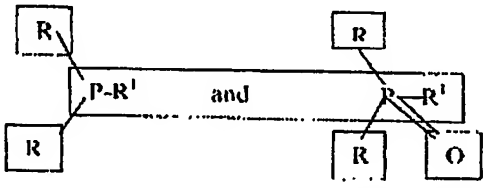
(3) Regarding the "reasoned statement" with respect to novelty, inventive step, and industrial applicability, the applicant argues that the claims have novelty and an inventive step because the phosphine and phosphine oxide dendrons do not have a quenching effect, as do the sulfer analogues. To support this argument, data from Example 21 (Figure 17) is cited. This argument is not convincing because, regardless of whether or not the phosphine and/or phosphine oxide dendrons are superior to analogous sulfer dendrons in terms of quenching effect, Peng et al. explicitly teaches using phosphine and phosphine oxide dendrons. Additionally, the data only shows a superior "lack of quenching" effect when very specific dendrons are used (i.e., citrate and Gen-2 polyether phosphine ligand 12). As such, the argument regarding superior results is not commensurate in scope with the claimed invention, which is open to phosphine and phosphine oxide based dendrons in general.

It is contemplated within the scope of this invention to include dendrimers other than disulfide type core dendrimers, such as, for example, those containing phosphorus atoms.

Contemplated within the scope of this invention are functional groups on the surface of the dendrimers/dendrons that are certain hydrophilic, hydrophobic, reactive or passive groups that include, by way of example such groups as: hydroxyl, amino, carboxylic, sulfonic, sulfonato, mercapto, amido, phosphino, -NH-COPh, -COONa, alkyl, aryl, ester, heterocyclic, alkynyl, alkenyl, and the like. The generation level of the dendrimer can range from about zero to ten.

The metal cores can be any semiconductor, metal or metal salt that will react with or adsorb the functional group of the dendrons, for example, but not limited to Au, Ag, Cu, Pt, Pd, Fe, Co, Ni, Zn, Cd, or their alloys; magnetic compositions such as Fe compounds, Fe_2O_3, Ni, and the like, metal salt and oxides/sulfides/selenides such as CdSe, CdS, CdSe/CdS, CdSe/ZnS, CdTe, CdTe/CdS, CdTe/ZnS, and such materials that have been passivated.

Contemplated within the scope of this invention are the above-mentioned materials wherein the core is bonded to the dendritic material with phosphorus-containing materials, such as phosphines, for example, aryl, alkyl and mixed aryl/alkyl phosphines and aryl, alkyl and mixed aryl/alkyl phosphine oxides. The phosphines are those having the formula:



wherein each R is independently selected from alkyl radicals having 1 to 4 carbon atoms and aryl groups, and R^1 is a functionally reactive connector group, for example a benzoic acid radical. Such materials are bound to the dendritic material and then, they bind through the phosphine to the quantum dot. (See Figure 3). The preferred materials are the aryl phosphines. These materials are stable in air and are less toxic than alkyl phosphines. The aryl groups that are UV active at 200 nm will not block any photoluminescence that is above 500 nm. Most importantly, phosphine passivation set forth above may not quench the photoluminescence that is essential for bio labeling.

AMENDED SHEET

What is claimed is:

1. A method of stabilizing semiconductor, metal, and metal salt nanoparticles, the method comprising contacting organic dendrons containing single focal point phosphine groups, with colloidal solutions of semiconductor, metal, and metal salt nanoparticles and allowing the single focal point phosphine groups to react with the surfaces of the semiconductor, metal, and metal salt nanoparticles to obtain stabilized, dendronized, semiconductor, metal, and metal salt nanoparticles.

2. A method of stabilizing nanoparticles selected from the group consisting of semiconductor, metal, and metal salt nanoparticles, the method comprising contacting organic dendrons containing single focal point phosphine oxide groups, with colloidal solutions of semiconductor, metal, and metal salt nanoparticles and allowing the single focal point phosphine oxide groups to react with the surfaces of the semiconductor, metal, and metal salt nanoparticles to obtain stabilized, dendronized, semiconductor, metal, and metal salt nanoparticles.

3. A method according to claim 1 wherein the semiconductor, metal, and metal salt nanoparticles are passivated prior to contacting them with the single focal point functional groups.

4. A method according to claim 2 wherein the semiconductor, metal, and metal salt nanoparticles are passivated prior to contacting them with the single focal point functional groups.

5. A method according to claim 1 wherein the outside surfaces of the dendrons contain functional groups.

6. A method according to claim 2 wherein the outside surfaces of the dendrons contain functional groups.

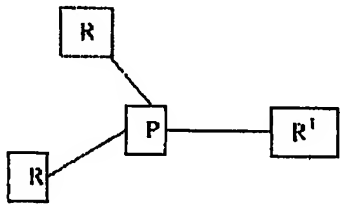
7. A method as claimed in claim 5 wherein the functional groups on the outside surfaces of the dendrons are selected from the group consisting of: (i) hydrophilic groups, (ii) hydrophobic groups, (iii) reactive groups, and (iv) passive groups.

AMENDED SHEET

8. A method as claimed in claim 6 wherein the functional groups on the outside surfaces of the dendrons are selected from the group consisting of: (i) hydrophilic groups, (ii) hydrophobic groups, (iii) reactive groups, and (iv) passive groups.

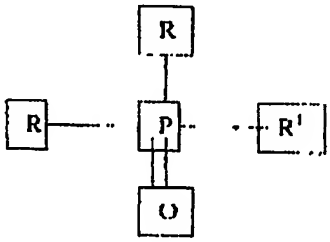
9. A method as claimed in claim 7 wherein the reactive groups are selected from the group consisting of: hydroxyl, amino, carboxylic, sulfonic, sulfonato, mercapto, amido, phosphino, -NH-COPh, -COONa, alkyl, aryl, ester, heterocyclic, alkynyl, and alkenyl.

10. A method as claimed in claim 1 wherein the phosphine group has the formula:



wherein each R is independently selected from alkyl radicals having 1 to 4 carbon atoms and aryl groups, and R^1 is a functionally reactive connector group.

11. A method as claimed in claim 2 wherein the phosphine oxide group has the formula:



AMENDED SHEET

wherein each R is independently selected from alkyl radicals having 1 to 4 carbon atoms and aryl groups, and R^1 is a functionally reactive connector group.

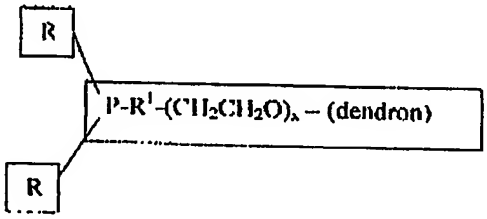
12. A composition of matter, said composition of matter being colloidal solutions selected from the group consisting of semiconductor nanoparticles, metal nanoparticles, and metal salt nanoparticles having outside surfaces, said outside surfaces having attached thereto, dendrons, said attachment comprising a linking group selected from:

phosphorus, wherein the phosphorous is in the form of a group selected from:

(a) phosphines, and

(b) phosphine oxides in combination with ethylene oxide units.

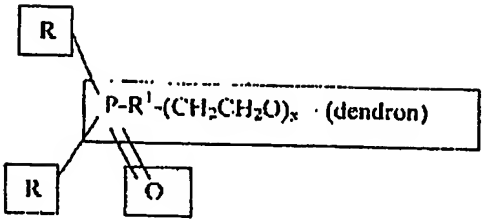
13. A composition of matter as claimed in claim 12 wherein (a) in combination with ethylene oxide has the general formula:



wherein x has a value of from 1 to 10, each R is independently selected from alkyl groups of 1 to 4 carbon atoms and aryl groups and R^1 is a connector group.

14. A composition of matter as claimed in claim 12 wherein (b) in combination with ethylene oxide has the general formula:

AMENDED SHEET



wherein x has a value of from 1 to 10, each R is independently selected from alkyl groups of 1-4 carbon atoms and aryl groups and R^1 is a connector group.

15. A composition of matter as claimed in claim 12 wherein the nanoparticle core is iron.

16. A composition of matter as claimed in claim 12 wherein the nanoparticle core is gold.

17. A composition of matter as claimed in claim 12 wherein the nanoparticle core is copper.

18. A composition of matter as claimed in claim 12 wherein the nanoparticle core is platinum.

19. A composition of matter as claimed in claim 12 wherein the nanoparticle core is palladium.

20. A composition of matter as claimed in claim 12 wherein the nanoparticle core is cobalt.

21. A composition of matter as claimed in claim 12 wherein the nanoparticle core is nickel.

22. A composition of matter as claimed in claim 12 wherein the nanoparticle core is zinc.

23. A composition of matter as claimed in claim 12 wherein the nanoparticle core is cadmium.

24. A composition of matter as claimed in claim 12 wherein the nanoparticle core is iron oxide.

AMENDED SHEET

25. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdSe.

26. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdS.

27. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdSe/CdS.

28. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdSe/ZnS.

29. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdTe.

30. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdTe/CdS.

31. A composition of matter as claimed in claim 12 wherein the nanoparticle core is CdTe/ZnS.

32. A composition of matter as claimed in claim 12 wherein the composition contains a drug, pharmaceutical or fragrance.

33. The use of the composition of matter of claim 15 as an MRI agent.

34. The use of the composition of matter of claim 16 as a projectile for a gene gun.

35. The use of the composition of claim 12 to carry a drug, pharmaceutical or fragrance.

36. The use of a composition of matter of claim 12 wherein the use is selected from the group consisting of: biologically active materials, genetic materials, biologically active materials for use as vaccines, biomedical tags, components in light emitting diode devices, diagnostics, nanosensors, nano-arrays for DNA and RNA, protein applications, chelators, photon absorption, energy absorbing, energy emitting, signal generator for diagnostics, and radioactive materials.

AMENDED SHEET